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User/Prescriber Leaflet

TETRAVAC®

Diphtheria, tetanus, acellular pertussis and inactivated poliomyelitis vaccine, adsorbed

Product Summary

TRADE NAME OF THE MEDICINAL PRODUCT

TETRAVAC®

Diphtheria, tetanus, acellular pertussis and inactivated poliomyelitis vaccine, adsorbed.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 millilitre dose of vaccine contains:

– Purified diphtheria toxoid . . . . . not less than 30 International Units#
– Purified tetanus toxoid . . . . . not less than 40 International Units*
– Purified pertussis toxoid (PTxd) . . . . . 25 micrograms
– Purified filamentous haemagglutinin (FHA) . . . . . 25 micrograms
– Inactivated type 1 (Mahoney) poliovirus D antigen **: . . . . . 40 units
– Inactivated type 2 (MEF-1) poliovirus D antigen **: . . . . . 8 units
– Inactivated type 3 (Saukett) poliovirus D antigen **: . . . . . 32 units

\# As mean value.
* As lower confidence limit (p = 0.95).
** Quantity of antigen in the final bulk product, in accordance with WHO recommendations.

Acetic acid or sodium hydroxide are used for pH adjustment as necessary.
The diphtheria and tetanus toxins obtained from cultures of *Corynebacterium diphtheriae* and *Clostridium tetani* are formaldehyde detoxified then purified.
The poliomyelitis vaccine is obtained from the propagation of poliomyelitis virus types 1, 2 and 3 on Vero cells, purified then inactivated by formaldehyde.
The acellular pertussis components (PT and FHA) are extracted from *Bordetella pertussis* cultures then separately purified. The pertussis toxin (PT) is detoxified with glutaraldehyde (PTxd). It then becomes the toxoid (PTxd). The FHA is native. It has been shown that PTxd and FHA are two components which are of importance in protection against pertussis.

PHARMACEUTICAL FORM

Suspension for injection.

Clinical Particulars

THERAPEUTIC INDICATIONS

Active immunisation against diphtheria, tetanus, pertussis and poliomyelitis:
- for primary vaccination in infants,
- for booster in children who have previously received a primary vaccination with a diphtheria-tetanus-whole-cell or acellular pertussis-poliomyelitis vaccine.

POSOLOGY AND METHOD OF ADMINISTRATION

Primary vaccination

Primary immunisation can be given as 3 doses at an interval of 1-2 months starting at the age of 2 or 3 months or as 2 doses at an interval of 2 months starting at the age of 3 months and a third dose at the age of 12 months.

Booster

A fourth dose should be administered within the second year of life to children who received TETRAVAC® (or a diphtheria-tetanus-whole-cell or acellular pertussis-poliomyelitis vaccine, whether mixed or not with the freeze-dried conjugate *Haemophilus influenzae* type b vaccine) as a three-dose primary series between the ages of 2-6 months.
More data (e.g. epidemiological, clinical trial follow up) are required to establish the need for additional doses of acellular pertussis vaccines.
TETRAVAC® can also be administered to children aged 5-6 years or 8-12 years who were previously immunised with a whole-cell vaccine (four doses).
TETRAVAC® must be administered intramuscularly. The recommended injection sites are the antero-lateral aspect of the upper thigh in infants and the deltoid muscle in older children.
The intradermal or intravenous routes must not be used. Do not administer by intravascular injection: ensure that the needle does not penetrate a blood vessel.

CONTRA-INDICATIONS

Vaccination should be postponed in the case of fever or acute illness.
Known hypersensitivity to any component of the vaccine or to pertussis vaccines (either acellular or whole-cell pertussis).
Evolving encephalopathy.

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE

As each dose may contain undetectable traces of glutaraldehyde, thiomersal, neomycin, streptomycin, and polymyxin B, caution should be exercised when the vaccine is administered to subjects with hypersensitivity to the latter substances.
Appropriate medical treatment must be readily available for immediate use in case of an anaphylactic reaction following injection.
The immunogenicity of the vaccine may be reduced by immunosuppressive treatment or immunodeficiency. It is recommended to postpone vaccination until the end of such treatment or disease. Nevertheless, vaccination of subjects with chronic immunodeficiency such as HIV infection is recommended even if the antibody response may be limited.
The course of vaccination should not be completed in subjects who have a history of severe reaction within 48 hours of a preceding injection with a vaccine containing a pertussis component:
– fever greater or equal to 40°C for no other apparent causes
– inconsolable, persistent crying lasting more than 3 hours
– convulsions with or without hyperthermia
– allergic reactions
– hypotonic hyporesponsive episode

INTERACTIONS WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION

Except in the case of immunosuppressive therapy (see "SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE"), no significant clinical interaction with other treatments or biological products has been reported. A specific interaction study has been done on co-administration of TETRAVAC®, used to reconstitute freeze-dried Act-HIB® vaccine, and MMR.

PREGNANCY AND LACTATION

Not applicable. This vaccine is intended only for paediatric use.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Not applicable.

UNDESIRABLE EFFECTS

When TETRAVAC® is administered as a primary series, the most frequently reported reactions include irritability (20.2%), local reactions at the injection site such as redness (9%) and induration ≥ 2 cm (12%).
These signs and symptoms usually occur within 48 hours following the vaccination and may continue for 48-72 hours. They resolve spontaneously without requiring specific treatment.
In some countries, TETRAVAC® may be indicated for administration to children aged from 5 to 12 years as a late booster. Reactions to TETRAVAC® in children in this age group are less or equally frequently reported than after administration of DTP-IPV (whole-cell pertussis) or DT-IPV, respectively, at the same age.

Common reactions (> 1%)
- Injection site reactions: redness, induration.
- Systemic reactions: fever ≥ 38°C, irritability, drowsiness, feeding and sleep, disturbances, diarrhoea, vomiting.

Less common reactions (0.1% to 1%)
- Redness and swelling ≥ 5 cm at the injection site, fever ≥ 39°C, prolonged inconsolable crying.

Rare reactions (< 0.1%)
- High fever (> 40°C).

Convulsions or hypotonic hyporesponsive episodes have not been reported following the use of TETRAVAC®, but have been reported for other pertussis vaccines. The absence of such reactions cannot absolutely be ruled out. No other serious vaccine-related adverse events were observed in controlled clinical trials on more than 6000 infants and 2000 children aged from 12 to 24 months and 230 children aged 5 to 12 years. The incidence of such reactions can be evaluated only after a much larger number of children have been vaccinated.
Rare oedematous reactions in the lower limbs have been reported with vaccines containing the conjugate *Haemophilus influenzae* type b vaccine. These reactions comprised oedema with cyanosis or transient purpura occurring within the first hours following vaccination and resolving rapidly and spontaneously without sequelae. These reactions were not accompanied by cardio-respiratory signs. One such case, however, was reported during clinical trials performed with diphtheria-tetanus-acellular pertussis-poliomyelitis vaccine (TETRAVAC®) administered simultaneously with the conjugate *Haemophilus influenzae* type b vaccine at two separate injection sites.

OVERDOSE

Not applicable.

Pharmaceutical Particulars

LIST OF EXCIPIENTS

Aluminium hydroxide (expressed as Al^{+++}) . . . . . 0.30 milligram
Formaldehyde . . . . . 12.5 micrograms
2-phenoxyethanol . . . . . 2.5 microlitres
Medium 199 in water for injection up to . . . . . 0.5 millilitre

Medium 199 is a complex mixture of amino acids (including phenylalanine), mineral salts vitamins and other substances (including glucose) diluted in Water for Injection.

INCOMPATIBILITIES

The vaccine should not be mixed with other medicinal products except Act-HIB® vaccine.

SPECIAL PRECAUTIONS FOR STORAGE

Store between + 2°C and + 8°C (in a refrigerator).
Do not freeze.

PACKAGE QUANTITIES

Prefilled single dose syringe (0.5 millilitre) of glass type I, with chlorobromobutyl rubber plunger.

INSTRUCTIONS FOR USE/HANDLING

Shake before using to obtain a homogeneous white turbid suspension.
TETRAVAC® can be used to dissolve the freeze-dried conjugate *Haemophilus influenzae* type b vaccine (Act-HIB®). Shake the prefilled syringe so that the contents become homogeneous. Add the suspension to the vial and shake carefully until the freeze-dried substance is completely dissolved. The suspension must be white turbid after reconstitution.

Administrative Data

MARKETING AUTHORISATION HOLDER

UK:
Aventis Pasteur MSD Limited
Mallards Reach
Bridge Avenue
Maidenhead
Berkshire
SL6 1QP

Ireland:
Aventis Pasteur MSD Limited
Belgard Road
Tallaght
Dublin 24

MARKETING AUTHORISATION NUMBER

UK - PL 6745/0100
Ireland - PA 544/33/1

DATE OF (PARTIAL) REVISION OF THE TEXT: September 2000

LEGAL CATEGORY

POM

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Aventis Pasteur MSD

Patient Information Leaflet

TETRAVAC®

Diphtheria, tetanus, acellular pertussis, and inactivated poliomyelitis vaccine, adsorbed

This leaflet is a summary of the information available about TETRAVAC®. It should be read by parents or guardians of children receiving TETRAVAC®. Please read the leaflet carefully and if anything is unclear or you want to know more, ask your doctor, health visitor or clinic nurse. Keep this leaflet; you may want to read it again.
TETRAVAC® is one of a general group of medicines called vaccines, which are used to protect against infectious diseases. This vaccine helps to protect against diphtheria, tetanus, pertussis (whooping cough) and poliomyelitis.

WHAT IS IN TETRAVAC®?

The active ingredients in this vaccine are purified diphtheria toxoid (at least 30 international units - an international unit (I.U.) is for measuring vaccine activity), purified tetanus toxoid (at least 40 international units), purified pertussis toxoid (25 micrograms - a very small amount), and 25 micrograms of a purified form of part of the *Bordetella pertussis* bacterium (filamentous haemagglutinin), inactivated polio virus type 1 (40 Units), type 2 (8 Units) and type 3 (32 Units). These active ingredients are attached to not more than 0.3 milligram of aluminium hydroxide to increase their effectiveness. This vaccine also contains 12.5 micrograms of Formaldehyde and 2.5 microlitres of 2-phenoxyethanol (both of these are preservatives).
There is also an inactive ingredient which is Medium 199, a mixture of amino acids (including phenylalanine), mineral salts, vitamins and other components (including glucose).
The vaccine may contain traces of the antibiotics neomycin, streptomycin and polymyxin B. It may also contain traces of thiomersal or glutaraldehyde.
TETRAVAC® is available as a single dose (0.5 millilitre) prefilled syringe.

HOW DOES TETRAVAC® WORK?

The vaccine contains three toxoids which are harmless versions of the toxins produced by the bacteria which cause diphtheria, tetanus and pertussis (whooping cough), and a purified form of part of *Bordetella pertussis* bacterium (the bacterium which causes whooping cough). It also contains 3 types of inactivated polio virus. When the vaccine is given to your child, the body's natural defences will produce protection against diphtheria, tetanus, pertussis, and polio.

WHO MAKES TETRAVAC®?

TETRAVAC® is made by Aventis Pasteur SA, 2, avenue Pont Pasteur, 69007, Lyon, France.
The company licensed to sell TETRAVAC® is Aventis Pasteur MSD Limited. Their address is Mallards Reach, Bridge Avenue, Maidenhead, Berkshire, SL6 1QP (in the UK) and Belgard Road, Tallaght, Dublin 24 (in Ireland).

WHAT IS TETRAVAC® FOR?

TETRAVAC® helps to protect preschool age children against the following serious diseases:
- Diphtheria - an infectious disease that affects the throat. The disease causes fever and a painful, swollen sore throat. It can also cause difficulty in breathing, damage to the heart and kidneys, and paralysis.
- Tetanus ('lock jaw') - a disease that causes spasm of the muscles, convulsions and inability to breathe.
- Pertussis (whooping cough) - an infectious disease that causes violent and uncontrollable outbursts of coughing, often followed by vomiting.
- Polio - an infectious disease which affects the nervous system and can cause paralysis.

TETRAVAC® is used to prevent your child from getting these diseases by protecting him or her against these diseases before he or she comes into contact with the bacteria or virus.

IS TETRAVAC® RIGHT FOR YOUR CHILD?

TETRAVAC® is for children over 2 months of age. To make sure that this vaccine is right for your child, it is important to tell your doctor or nurse if any of the points below apply to your child. If there is anything that you do not understand, ask your doctor or nurse to explain.
Tell your doctor or nurse if your child:
- has ever had an allergic reaction (anaphylaxis) to a previous injection of a vaccine containing diphtheria and/or tetanus and/or pertussis, and/or acellular pertussis vaccine, and/or polio or any of the ingredients in TETRAVAC®. Symptoms of this are an itchy generalised skin rash (urticaria), swelling of the face and throat (angioedema), difficulty in breathing (dyspnoea), blue discolouration of the tongue or lips (cyanosis), low blood pressure (hypotension) and collapse.
- has ever had an allergic reaction to any of the following antibiotics: neomycin, streptomycin or polymyxin B. There may be traces of these in the vaccine.
- has an infectious illness (e.g. temperature, sore throat, cough, cold or flu), because your child's vaccination may need to be delayed until after they have recovered.
- was born with brain damage. In such cases vaccination can be given, unless your child's problems are getting worse, in which case vaccination should be delayed until your child's condition is stable. If your child has a stable condition such as cerebral palsy or spina bifida, vaccination can be given.
- has problems with his or her immune system, such as caused by AIDS, or has had a positive test for human immunodeficiency virus (HIV). Such children may be given TETRAVAC®, but the response to the vaccine may not be as good as in other children.
- has any blood disorders such as haemophilia (a condition where you bruise or bleed easily), because he or she may get bleeding at the injection site.

HOW WILL TETRAVAC® BE GIVEN?

The vaccination should be given in a suitable setting where staff are equipped to deal with any uncommon severe allergic reaction.
Your nurse or doctor will shake the vaccine before injecting it, usually into your child's leg or arm into a muscle. TETRAVAC® must not be injected into the skin.
Your doctor or nurse may make a note of the details of the injection.

The first course of vaccination

If your child has never had vaccination against diphtheria, tetanus, pertussis or polio before, he or she will need three injections of 0.5 millilitre TETRAVAC® with an interval of at least four weeks between the first and second doses, and at least four weeks between the second and third doses.
If acellular pertussis vaccine is not suitable for your child or if you do not wish him or her to have this part of the vaccine you should inform your doctor.

DOES TETRAVAC® HAVE ANY SIDE-EFFECTS?

After the injection the area around the injection site may become red, swollen, tender or painful. If this involves most of the upper part of the thigh, or arm (depending on where the vaccine was injected), tell your doctor.
A persistent hard lump or nodule may be felt under the skin at the site of the injection, especially if the injection was not very deep.
Less commonly your child may develop a temperature of 39°C or more (very rarely 40°C or more) within 48 hours of receiving the vaccine, be irritable, drowsy, have disturbed feeding and sleeping patterns, diarrhoea or vomiting. If these symptoms are troublesome or persist, call your doctor.
If your child cries inconsolably, or develops a high pitched scream lasting for more than four hours, consult your doctor.
Convulsions (fits) have not been reported after vaccination with TETRAVAC® but the possibility of their occurrence can not be entirely excluded. If you think your child is developing a fit, consult your doctor IMMEDIATELY.
A small number of patients have an allergic reaction to TETRAVAC®. This may cause an itchy generalised skin rash. Rarely the allergic reaction is very bad causing swelling of the face and throat, difficulty in breathing, blue discolouration of the tongue or lips, low blood pressure (causing dizziness) and collapse. If any of these symptoms or signs develop, consult your doctor IMMEDIATELY.
If you notice any other unpleasant effects after the vaccination that are not mentioned here, tell your doctor or nurse.

LOOKING AFTER TETRAVAC®

The vaccine should be stored in a refrigerator between + 2°C and + 8°C (making sure that it does not freeze), so that it keeps its effectiveness. The vaccine should not be used after the 'Expiry' date on the box. The vaccine should be shaken well before use, and should not be used if it is discoloured or large particles can be seen in it.

Date leaflet last revised: September 2000

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V3

APMSD 21/02/2001 MAC AMN14374/914970
(Haas - Futura - Futura Pasteur)
Aventis Pasteur MSD
Notice IRLANDE
Format à plat : 150 x 264 mm
Format plié : 150 x 22 mm
Code article : 914970
3 couleurs :
Gris PMS 445 C (Texte + 1/2 Logo tramé à 60 %)
Purple C (Bandeaux avec texte en réserve blanche)
Orange PMS 021 C
(Bandeau DCI avec texte en réserve blanche)
Pré-découpe sur pointillé

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